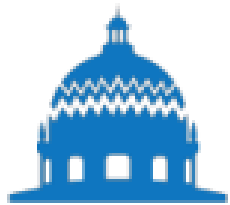


# HPV Vaccination as Population-Based Cancer Prevention

*Francisco García, MD, MPH*

*Director & CMO*

*Distinguished Outreach Professor of Public Health*



**PIMA COUNTY**  
HEALTH DEPARTMENT

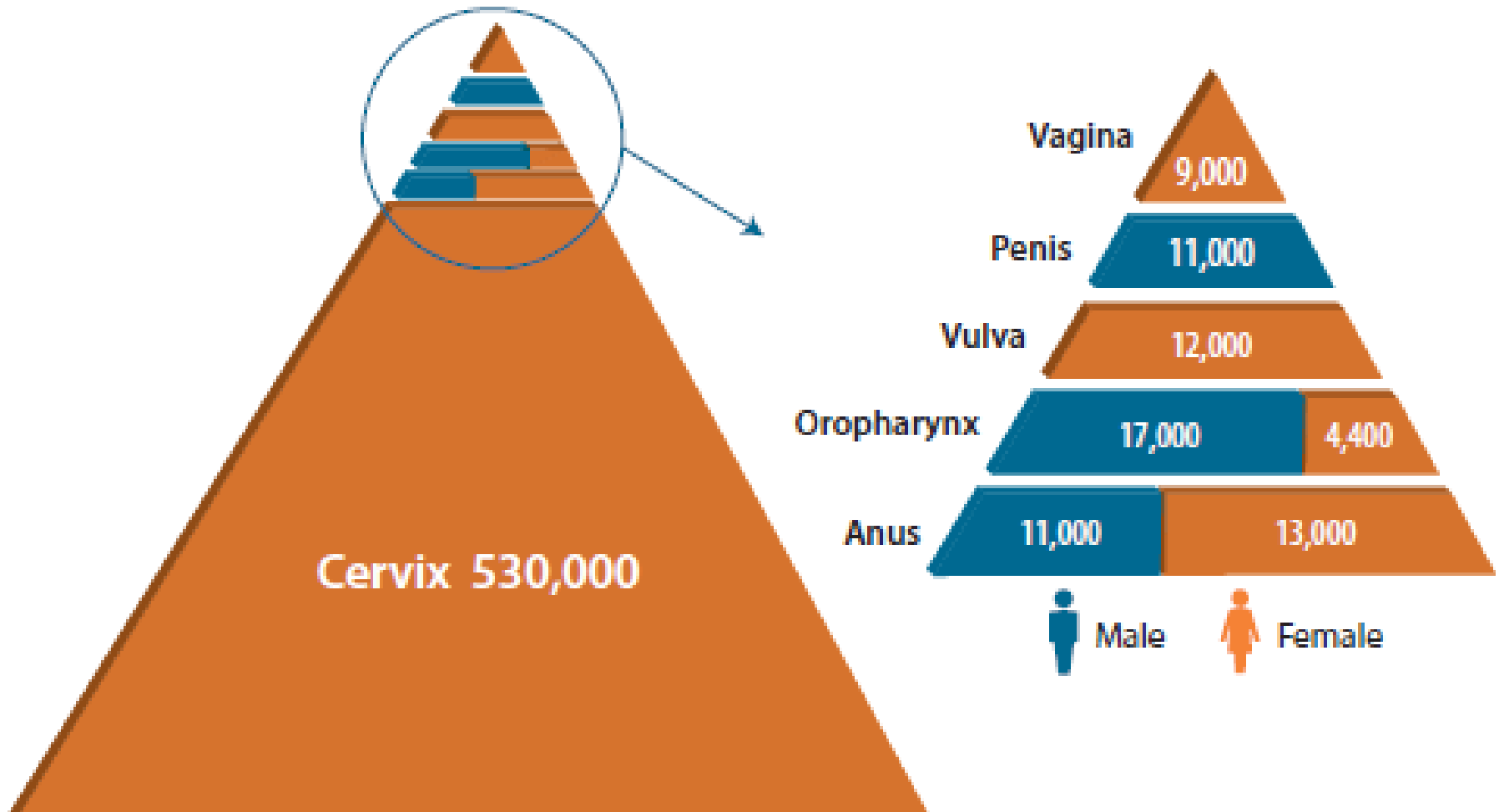
**A Healthy Pima County**  
Every **one**. Every **where**. Every **day**.

# Objectives

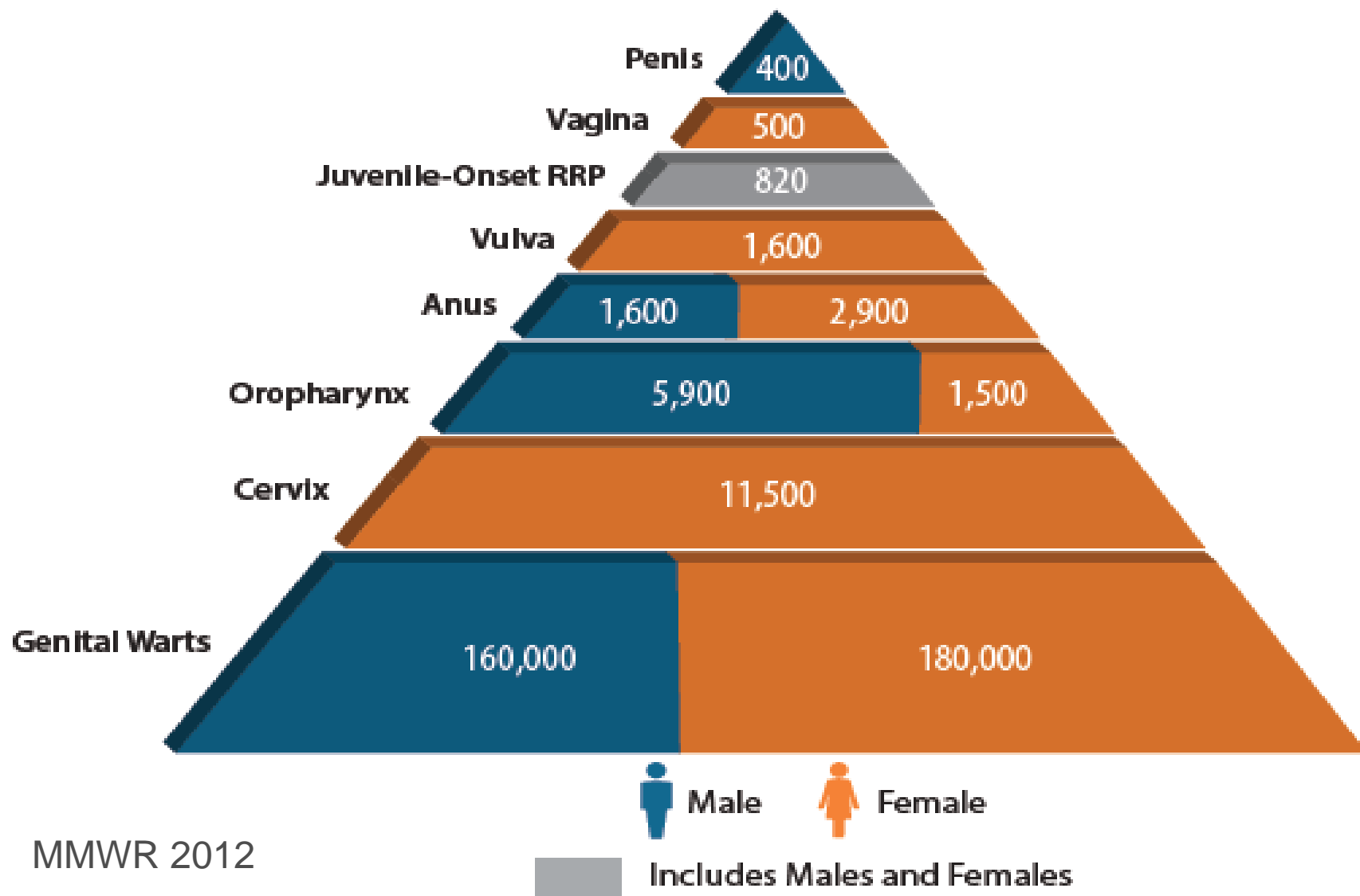
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- Review current understanding of epidemiology and natural history HPV infection and cervical cancer precursor
  - Discuss the evolution of screening guidelines and their application to the public health setting
  - Will NOT review/comment on primary screening data HPV test under review
-

# Global Estimate of HPV Attributable Cancer Burden--2008



# HPV Attributable Ca & EGWs: US 2004-2008



# HPV Attributable Cancers

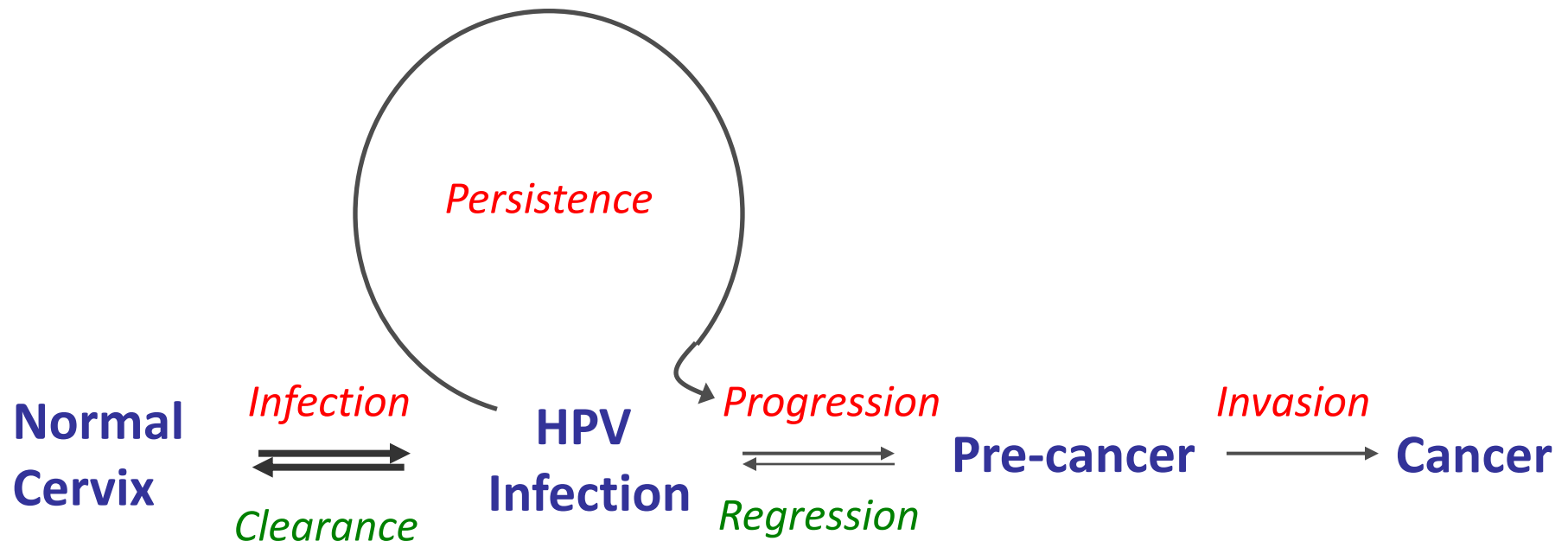
Cancer Site	Average # Cancers Per Year at Site (a)	Percent Probably Caused by HPV (a)	Number Probably Caused by HPV (a)	Percent HPV Cancers Probably Caused by HPV16 or 18 (b)	Number of Cancers Per Year Probably Caused by HPV16 or 18
Anus	4,767	93	4,500	93	4,200
Cervix	11,967	96	11,500	76	8,700
Oropharynx	11,726	63	7,400	95	7,000
Penis	1,046	36	400	87	300
Vagina	729	64	500	88	400
Vulva	3,136	51	1,600	86	1,400
<b>TOTAL</b>	<b>33,371</b>		<b>25,900</b>		<b>22,000</b>

(a) Centers for Disease Control and Prevention. Human papillomavirus-associated cancers—United States, 2004–2008. MMWR. 2012 Apr 20;61(15):258–61.

(b) Gillison ML, Chaturvedi AK, Lowy DR. HPV prophylactic vaccines and the potential prevention of noncervical cancers in both men and women. Cancer. 2008;113(10 Suppl):3036–46.

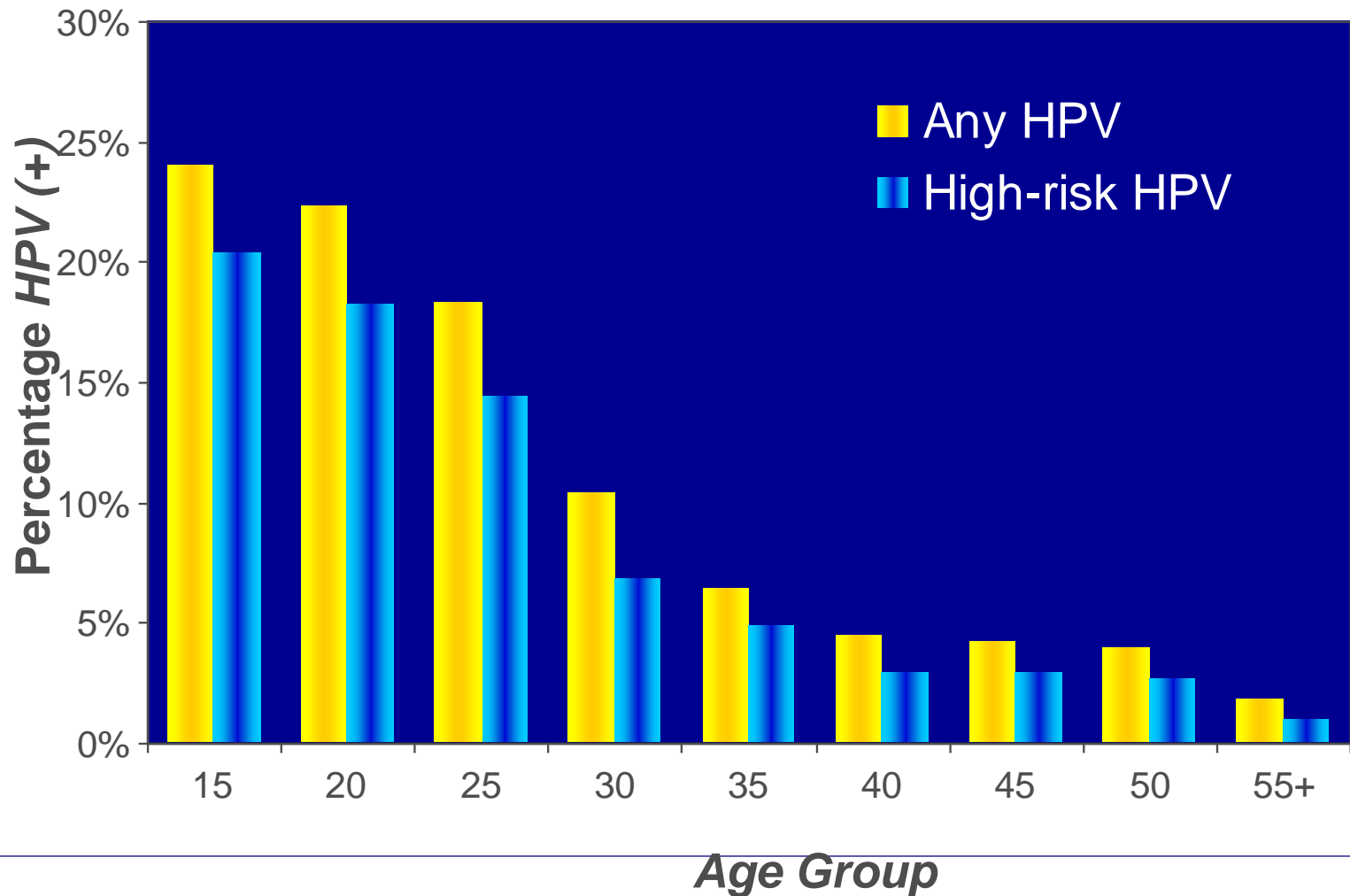
# Natural History of HPV Infection & Cervical Cancer

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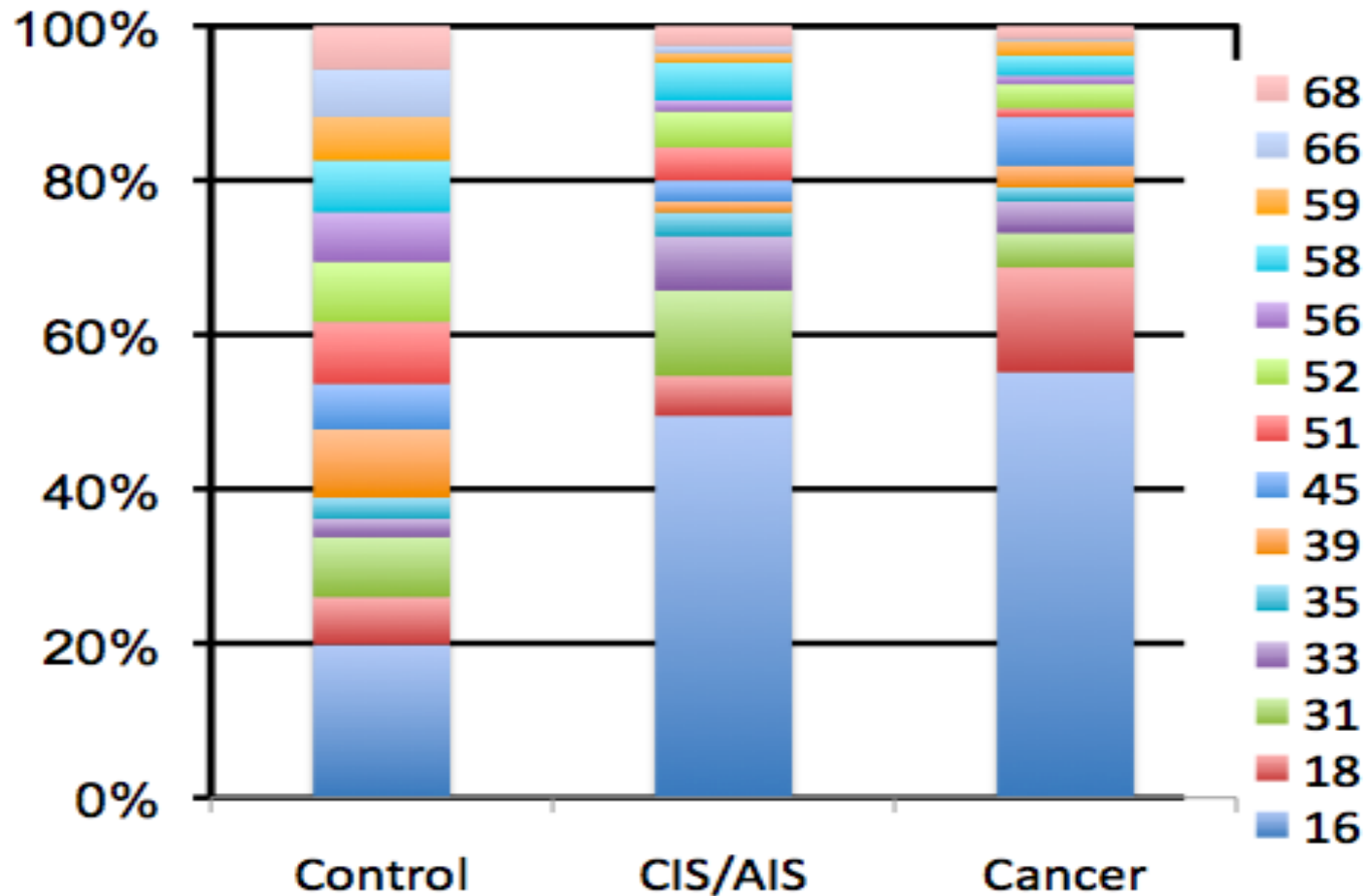


# HPV Positivity by Age

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# HPV Distribution in Cervical Cancer, CIN3, and Normal Cytology





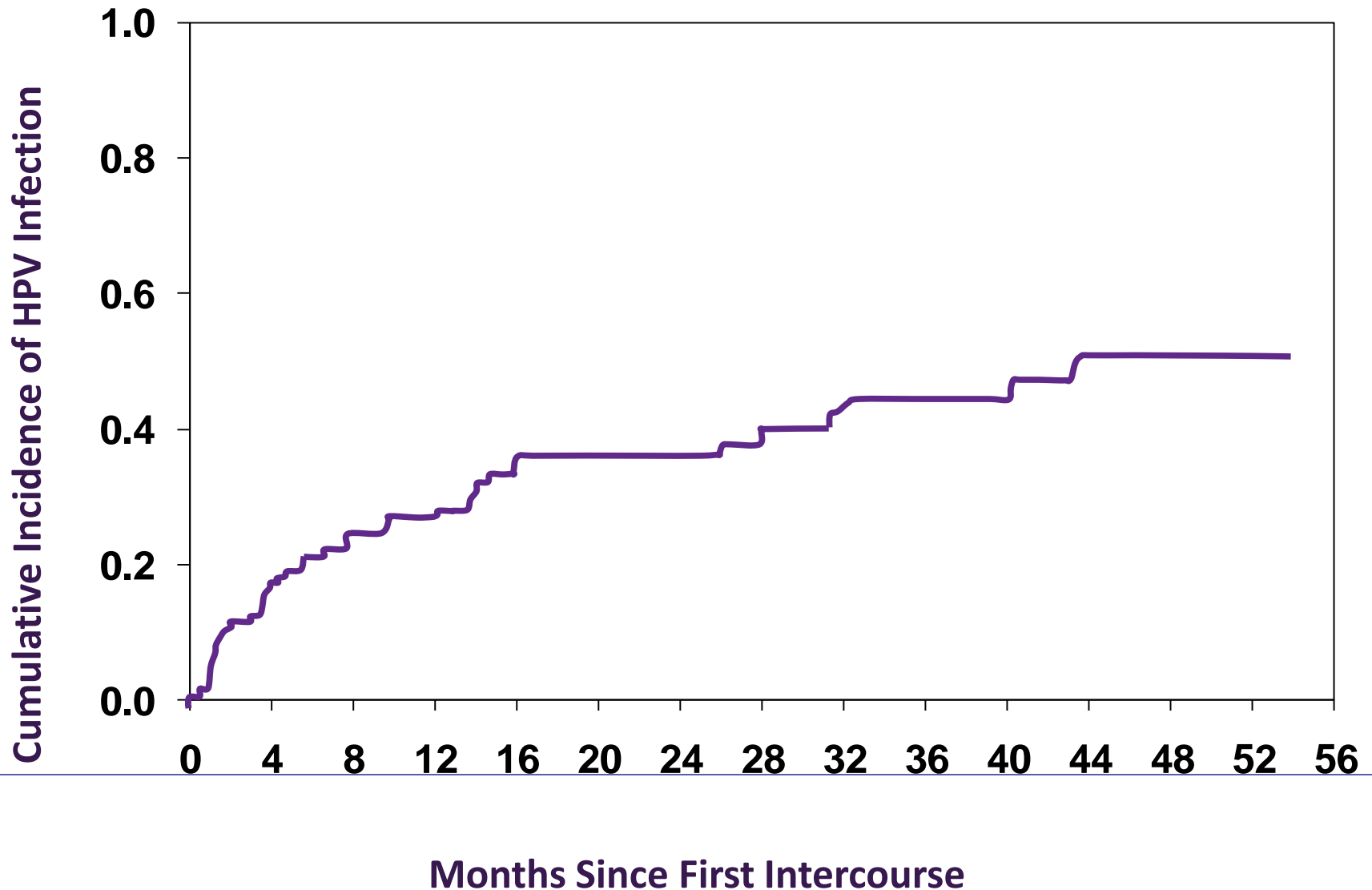
# Proportional Impact of HPV 16/18 and Other Viral Types by Tumor Type

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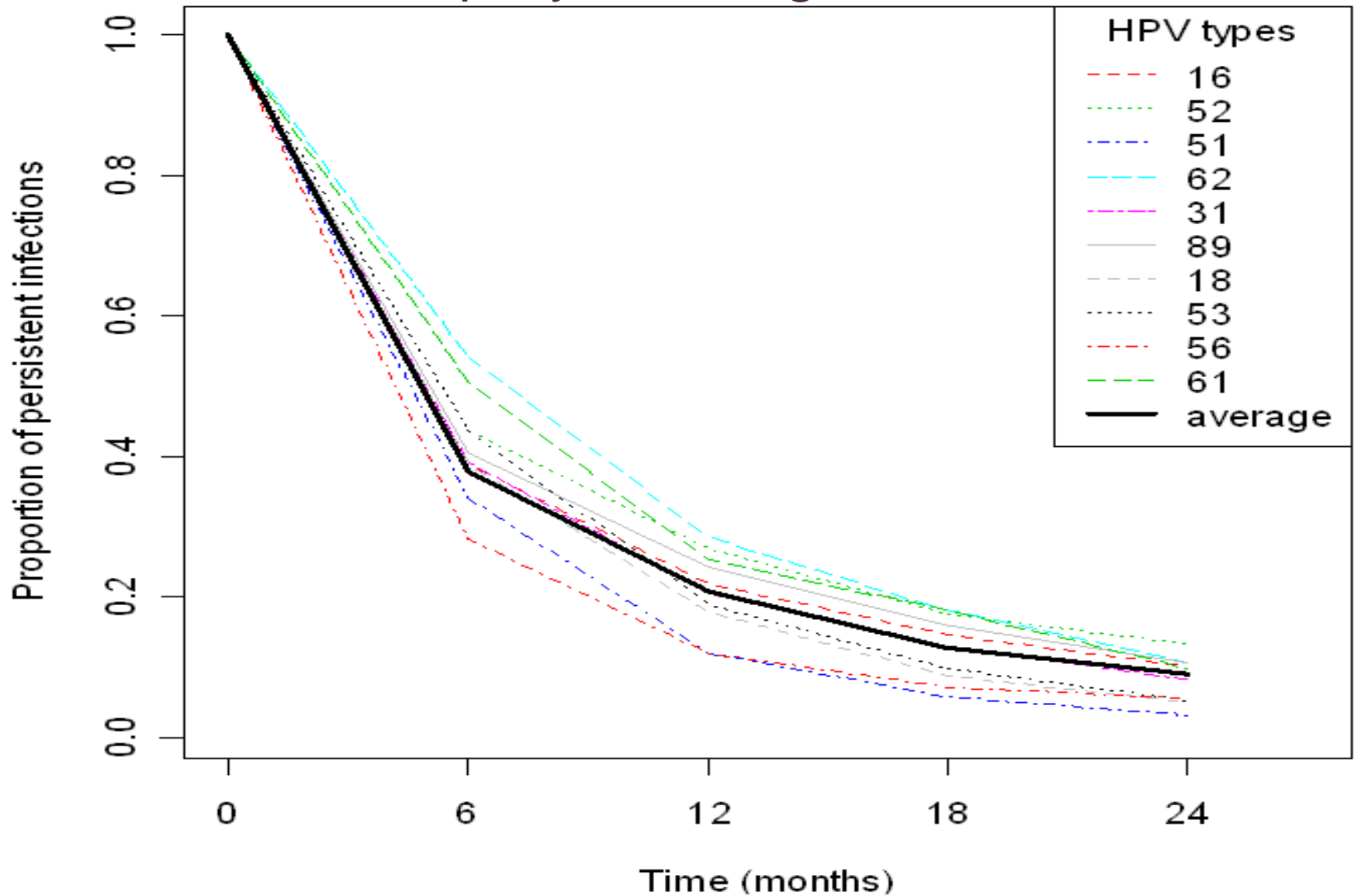


# Infection From Time of First Sexual Intercourse (Winer 2003)

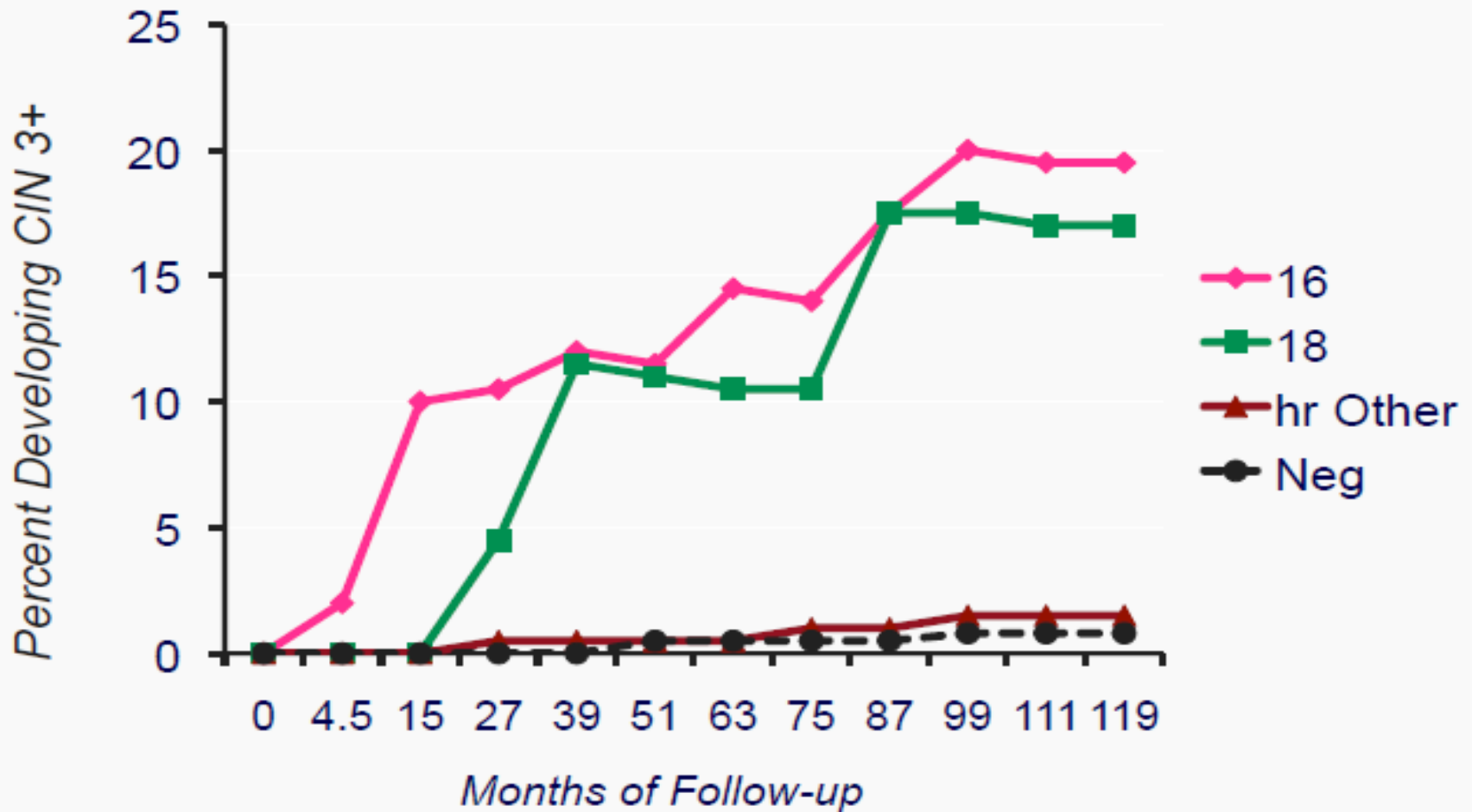
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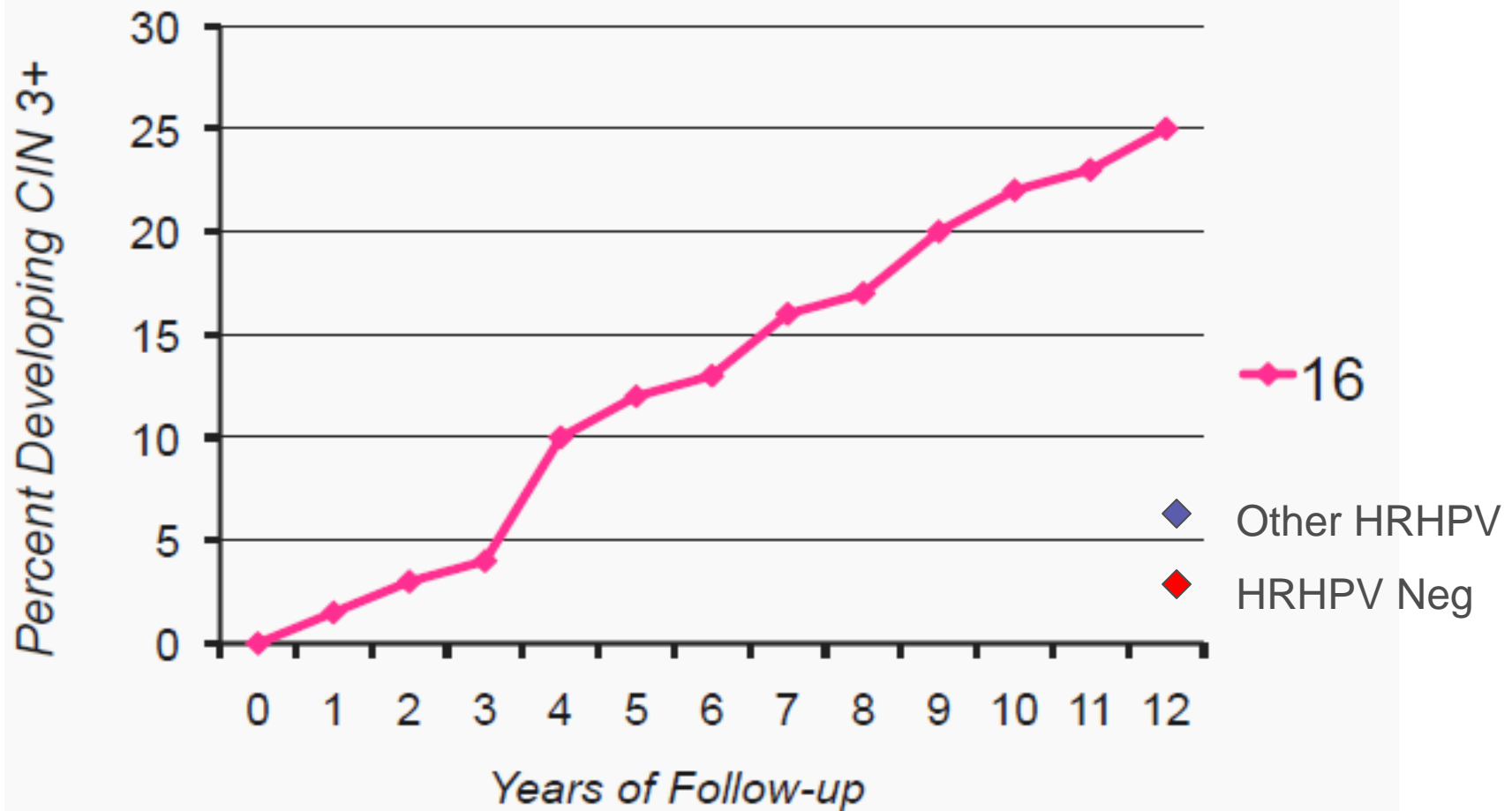
# Prevalent HPV Infections Resolve Spontaneously and Rapidly in Young Women



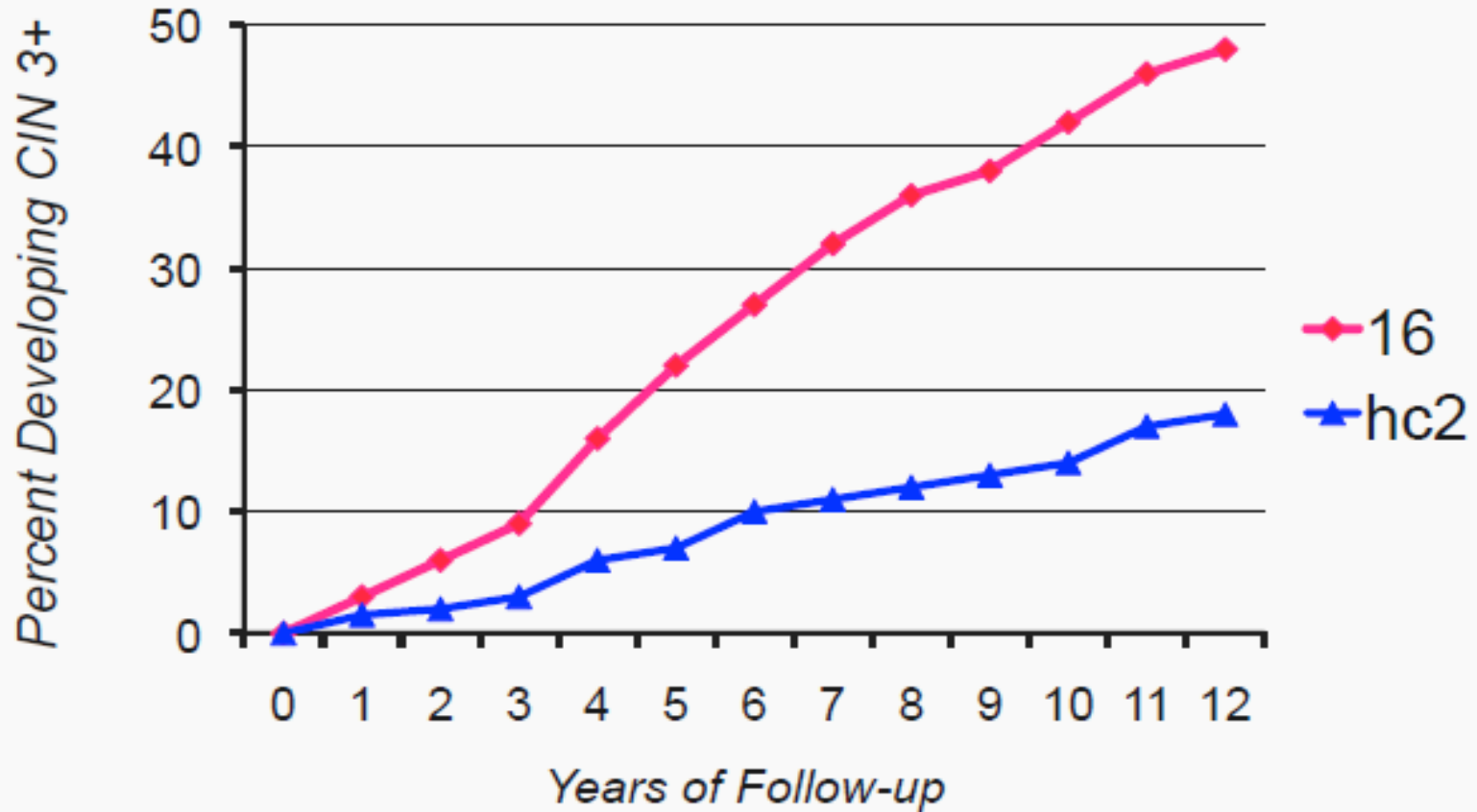
# Kaiser Portland Study: Risk of CIN3+ in Women $\geq 30$ with NILM Baseline



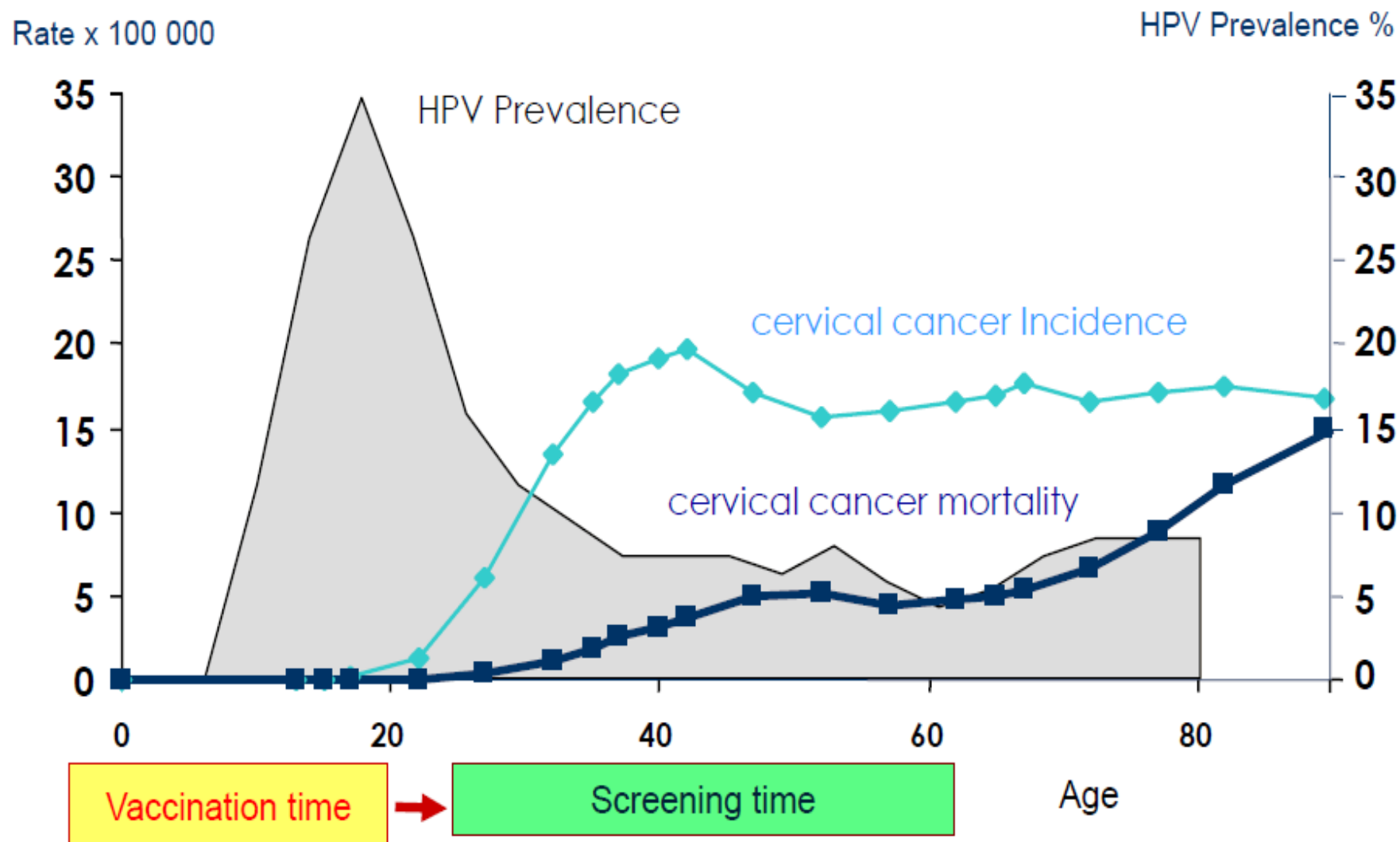
# Danish F/U Study: Long-term CIN 3+ Risk in NILM Cyto by HRHPV Status



# Long-term CIN3+ Risk with Persistent HRHPV Infection

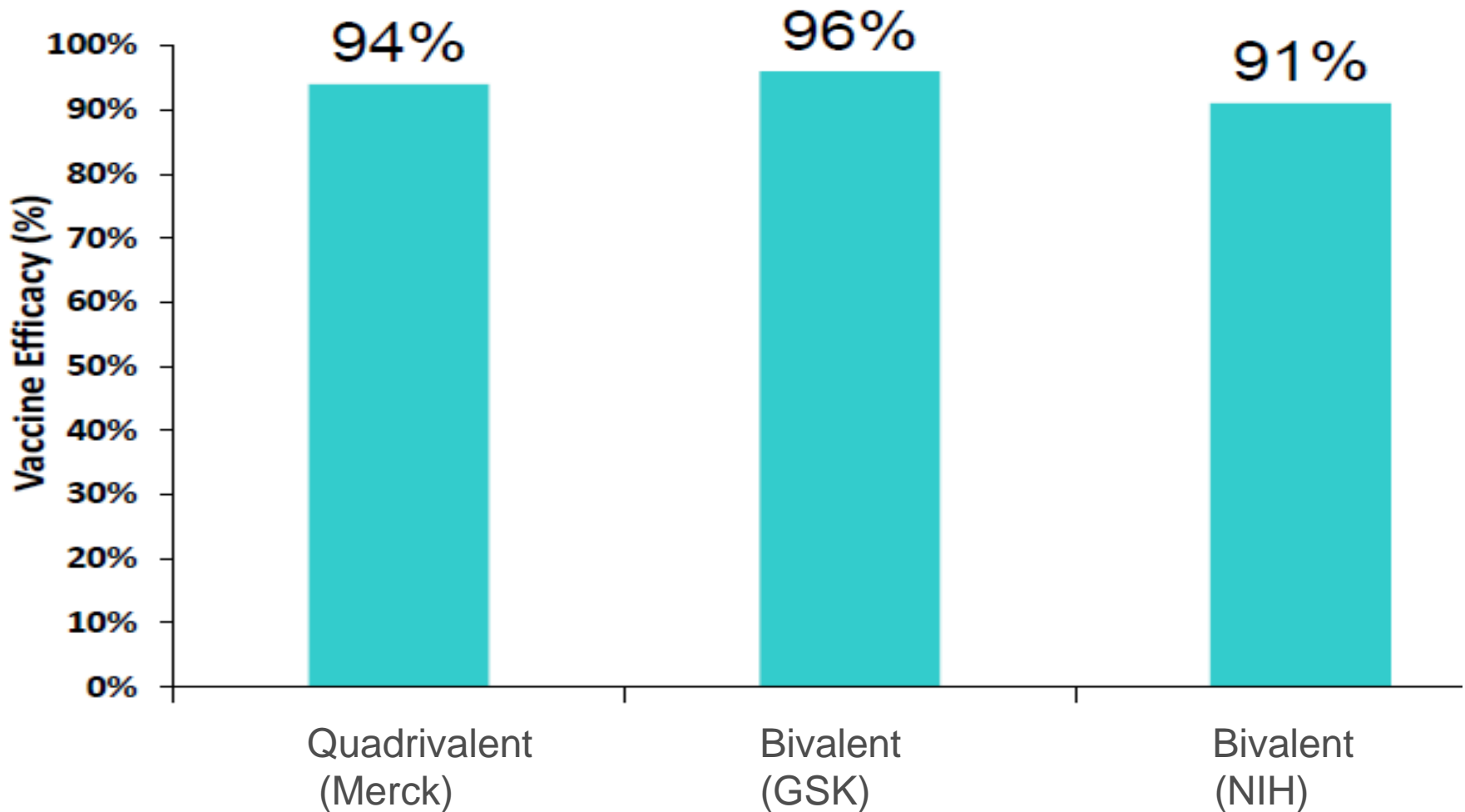


## HPV INFECTION AND DISEASE PROFILES AMONG WOMEN: DATA FROM FRANCE



# Efficacy of HPV Vaccine (per protocol) Results Across Trials

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Villa L. BMJ 2006; Paavonen J. Lancet 2009; Herrero R. Cancer Disc 2011



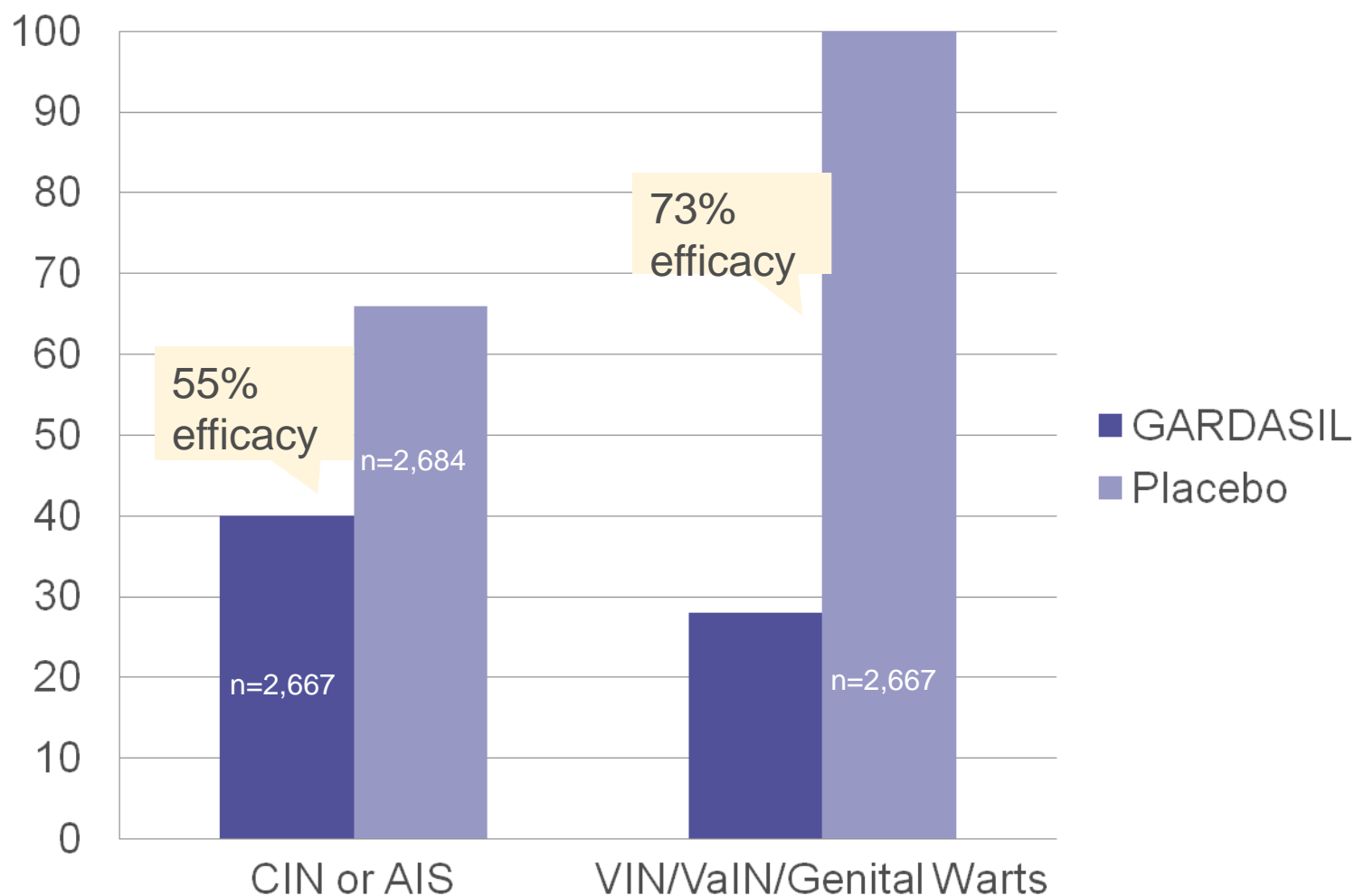
# Quadrivalent Phase III Trials: Future I Intention-to-Treat Population

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Intention-to-treat population

- Includes all women studied
- Demonstrates vaccine effectiveness in general population

# Prophylactic Efficacy for HPV 6/11/16/18–Related CIN/AIS, VIN/VaIN/Genital Warts Intent to Treat Population



# CRVT: Bivalent Vaccine Efficacy in Women

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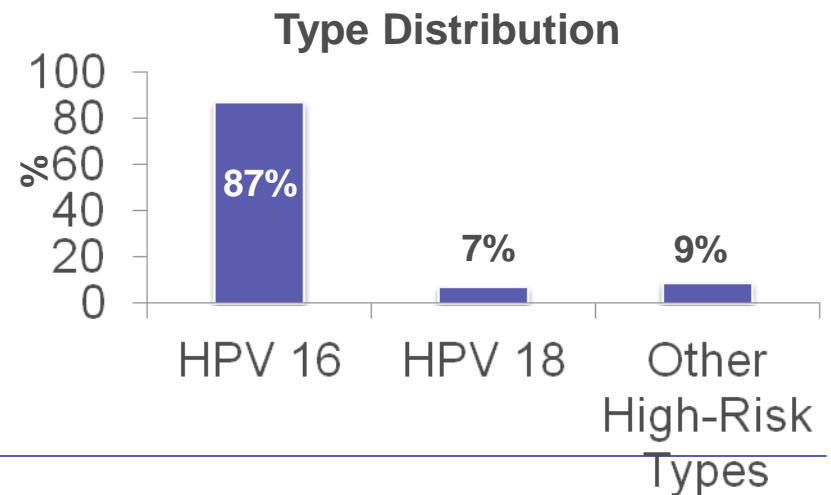
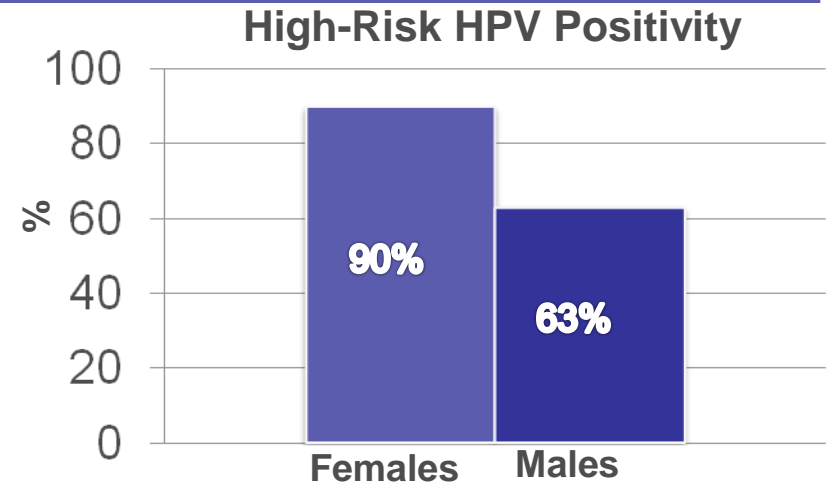
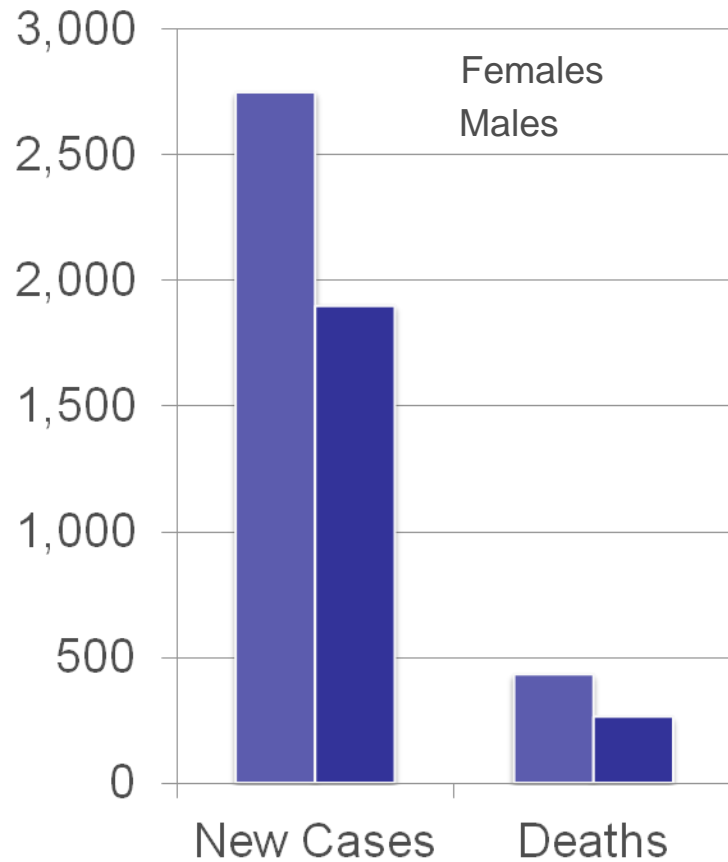
<i>Site</i>	<i>Study Arm</i>	<i>n</i>	<i>Persistent HPV 16/18</i>	<i>Efficacy (95% CI)</i>
Anus	HPV2	1003	8	84% (67-93)
	Control	986	48	
Cervix	HPV2	1003	10	88% (77-94)
	Control	986	81	

Kreimer, Lancet Onc 2011

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- 
- Bivalent vaccine strongly protects against anal HPV16/18 infections in women
  - Comparable to cervix
  - Will this translate to less anal cancer?
  - Does this apply equally to boys/men?
-

# HPV & Anal Cancer



# Efficacy Against HPV 6/11/16/18– Related Anal Disease Among MSM

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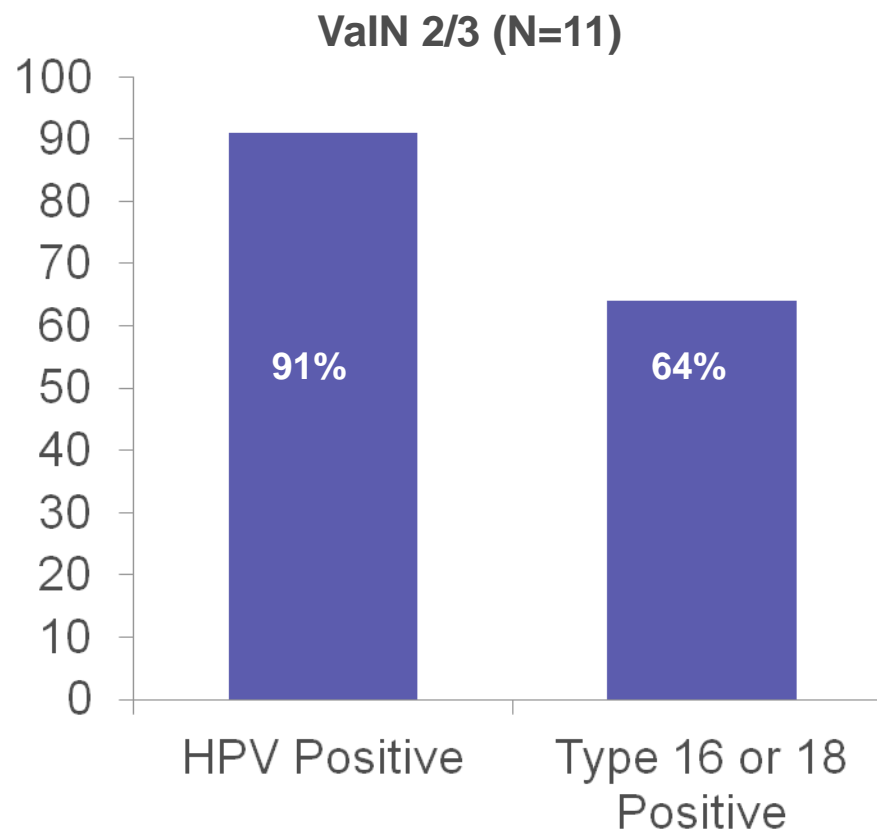
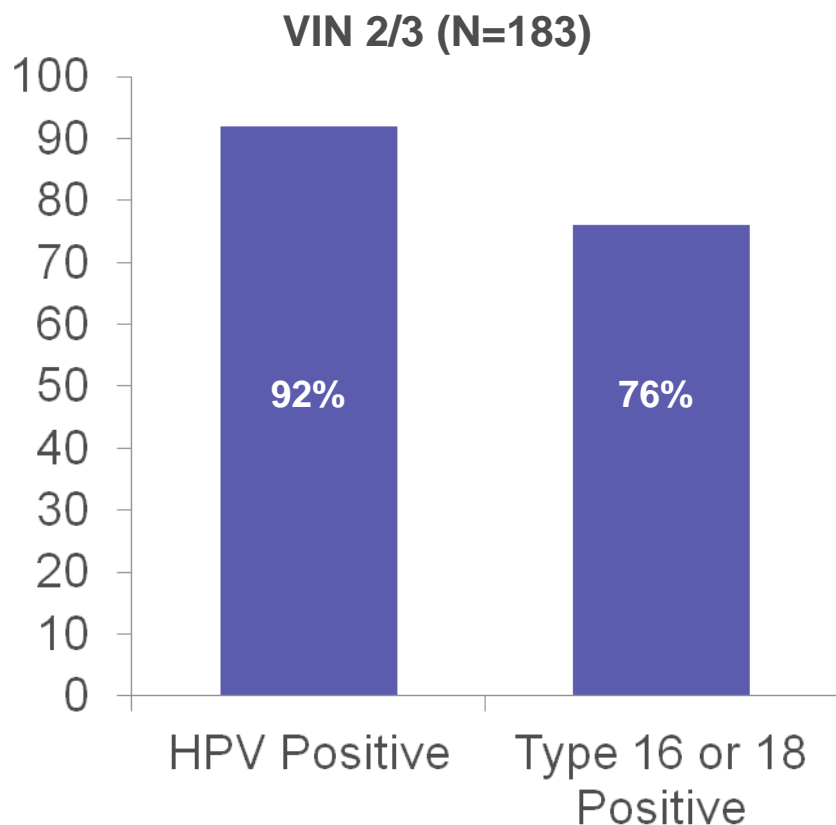
## Per-protocol population

	qHPV vaccine (n=299)		Placebo (n=299)		% Efficacy	95% CI	<i>P</i> value
Endpoint	Cases	Inc. per 100 PY	Cases	Inc. per 100 PY			
All subjects	5	1.3	24	5.8	<b>77.5</b>	39.6– 93.3	<0.001

- Anal intraepithelial neoplasia
  - Case counting began at month 7
-

# HPV & VIN/VaIN

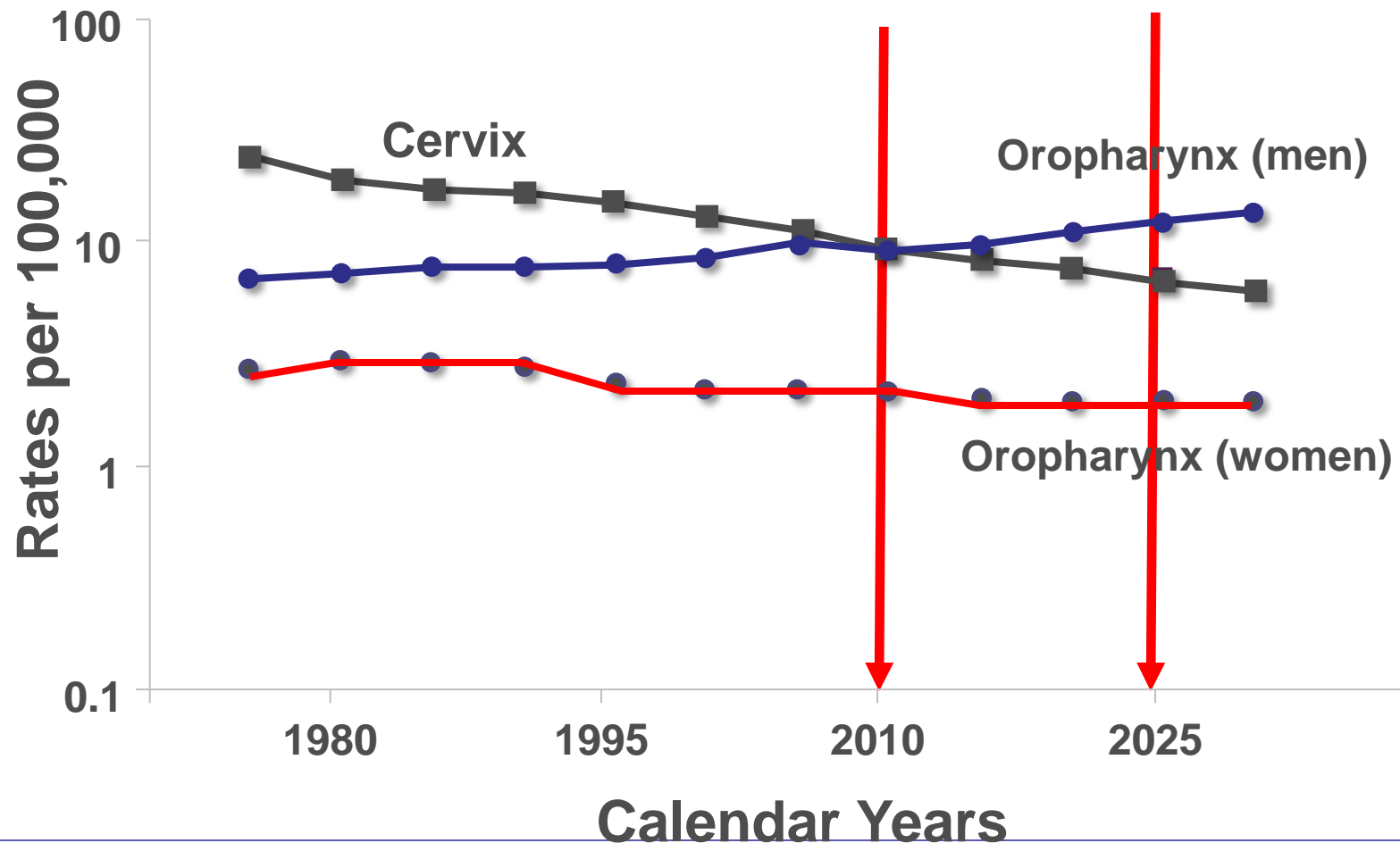
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**From a study of 241 women in Germany, diagnosed with lower genital tract dysplastic lesions.**

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# Observed & Projected U.S. Incidence Rates for Oropharyngeal Cancers v. Cervical Cancer





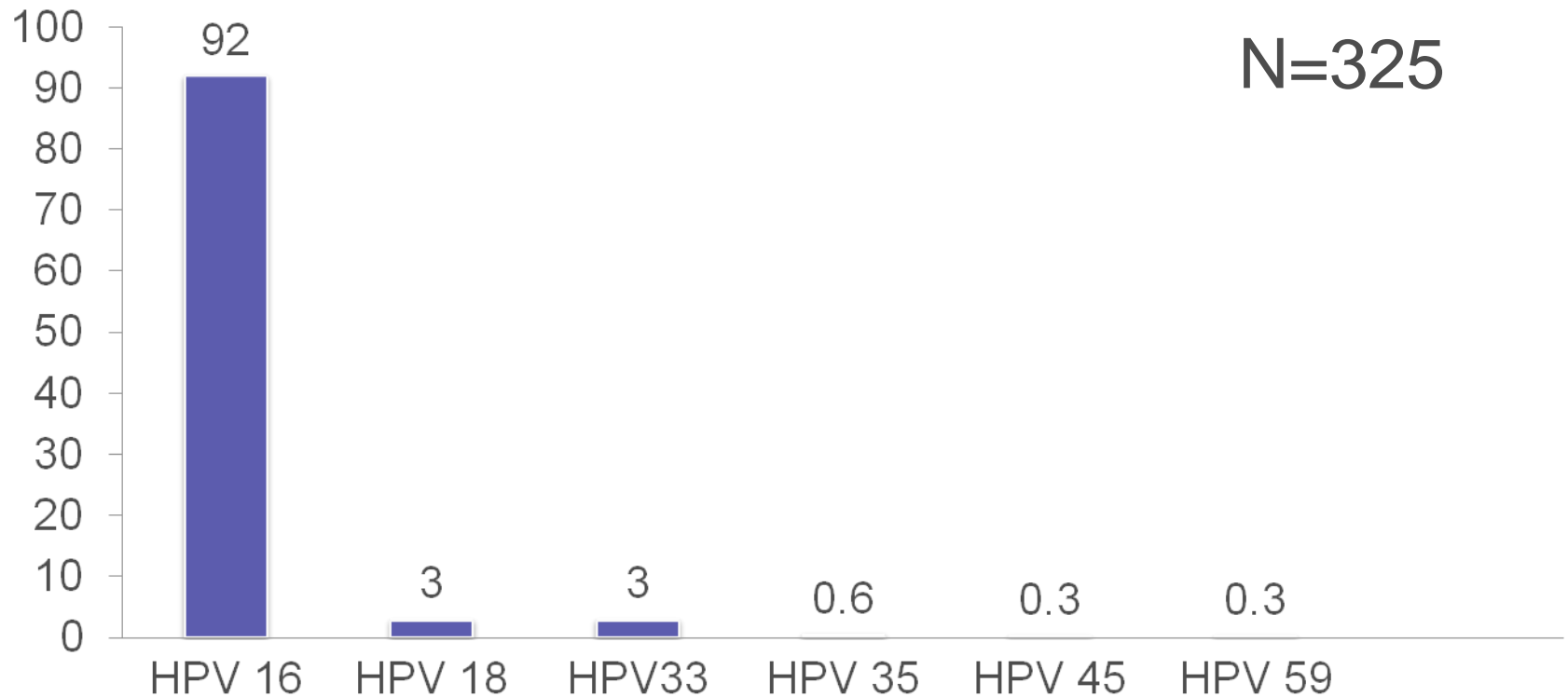
# HPV OP Natural History

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- Currently poorly defined
  - Believed to be sexually acquired
  - Associated with sexual behavior <sup>1,2</sup>
  - Questions largely unknown:
  - Duration of infection
  - Degree of oral transmission
  - Whether productive viral infections are established in the oropharynx
-

# Type Distribution of HPV+ Oropharynx Cases

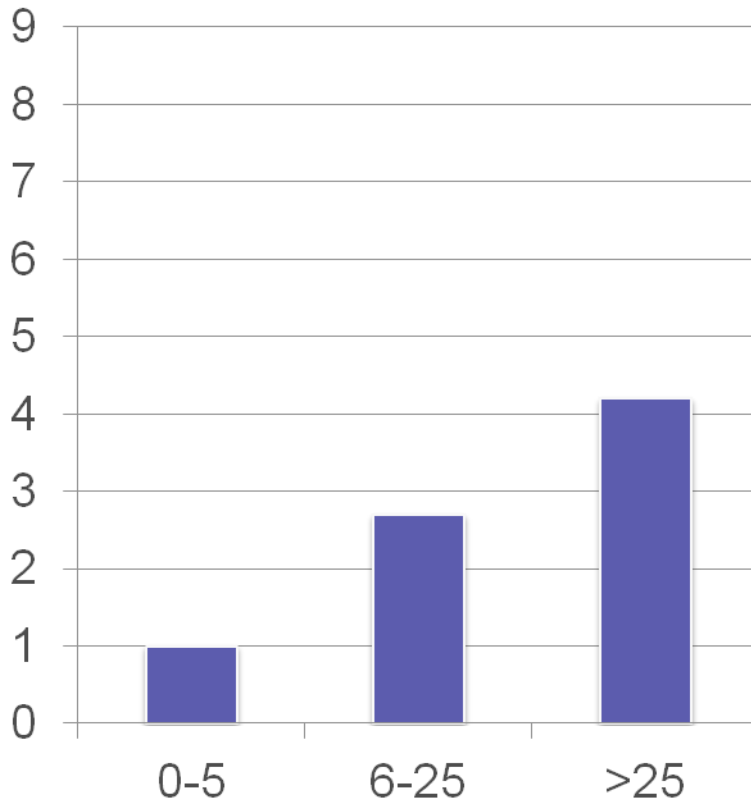
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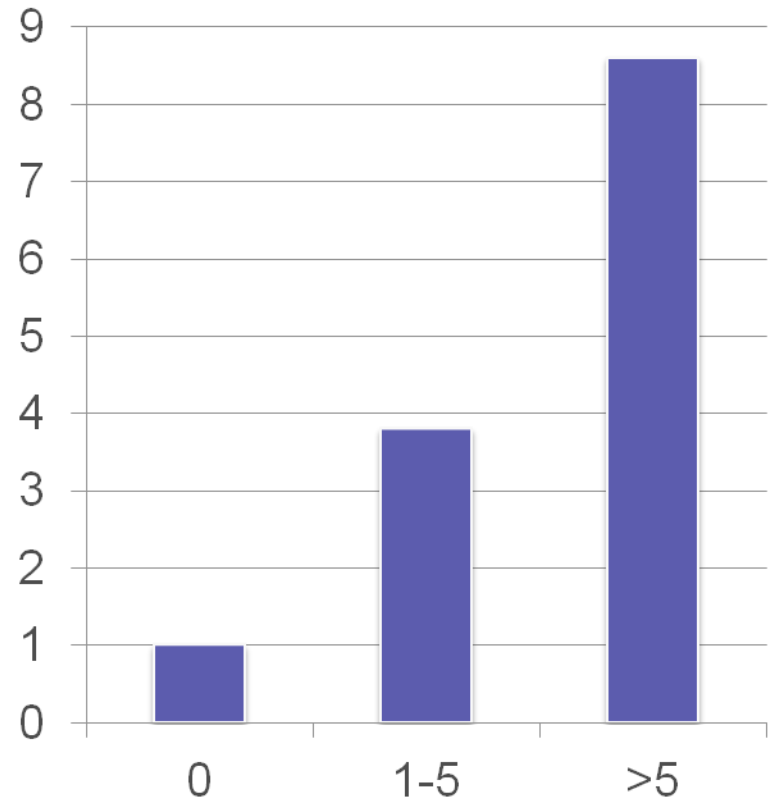
# HPV+ and Sexual Behavior

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**# Sex Partners**

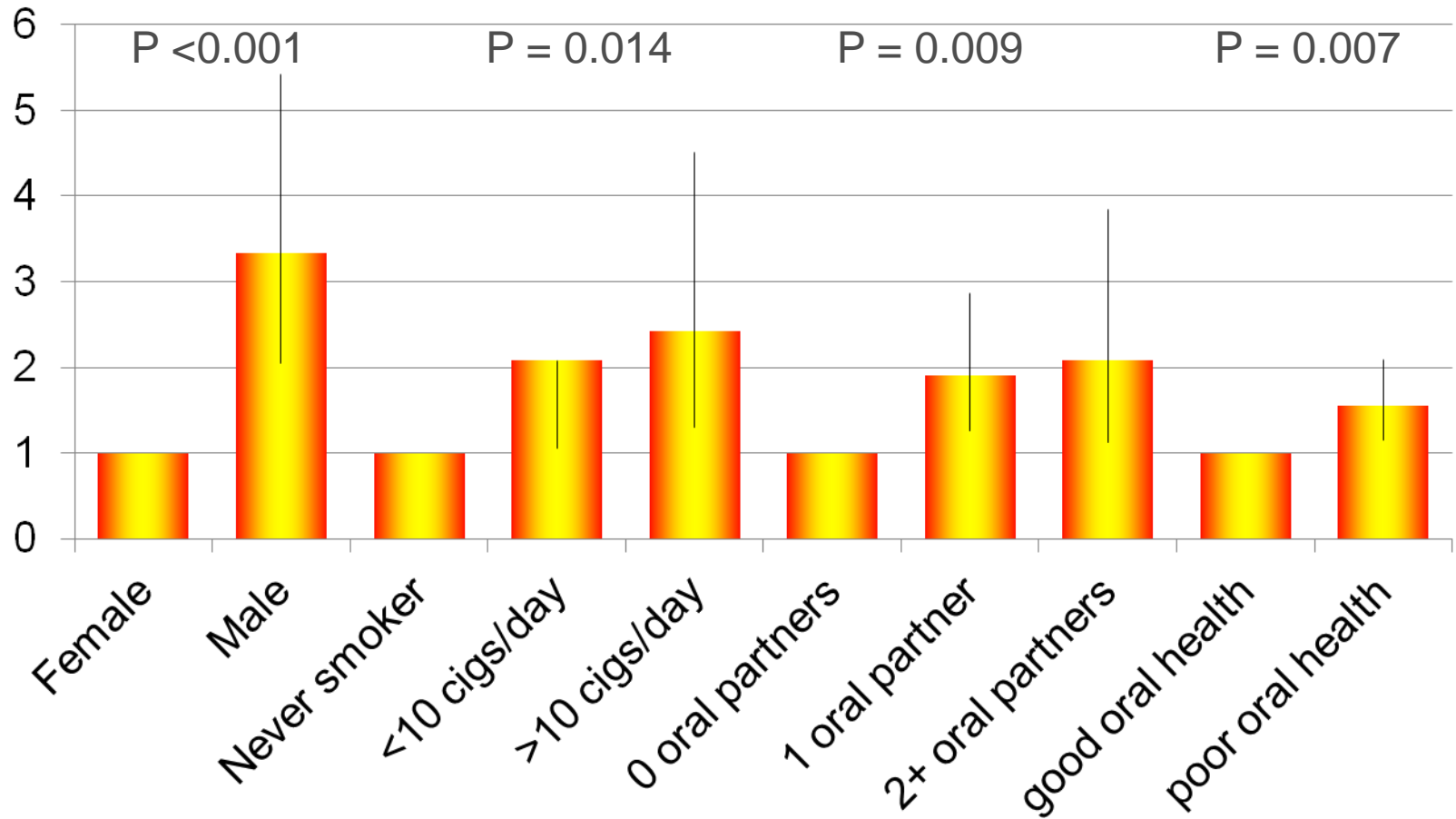


**# Oral Sex Partners**



OR - Adjusted for age, gender, tobacco, alcohol, family Hx, and dental hygiene

# Adjusted Odds Ratios for Oral HPV Infection



N = 3,439 age 30 - 69 years from the 2009–2010 NHANES Survey

# Conclusion

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- Cervical cancer prevention efforts must balance safety and potential benefit
  - New guidelines based on improved understanding of the disease process and limitations of screening
  - Policy decisions must be made from a societal perspective, while clinical choices reflect individual preferences and perception of risk
  - *Primum non nocere*
-

*Francisco.Garcia @Pima.Gov*



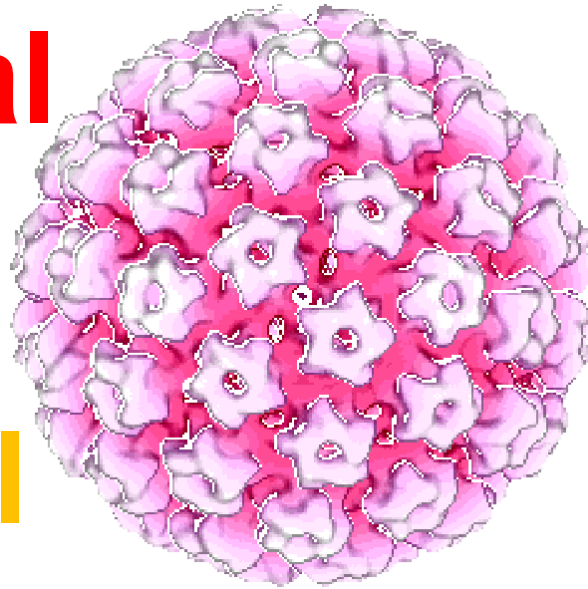
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# HPV and Cancer

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**Cervical**

**Anal**



**Head &  
Neck?**

**What is the common thread?**



# Metaplasia happens





# Epithelia Transition

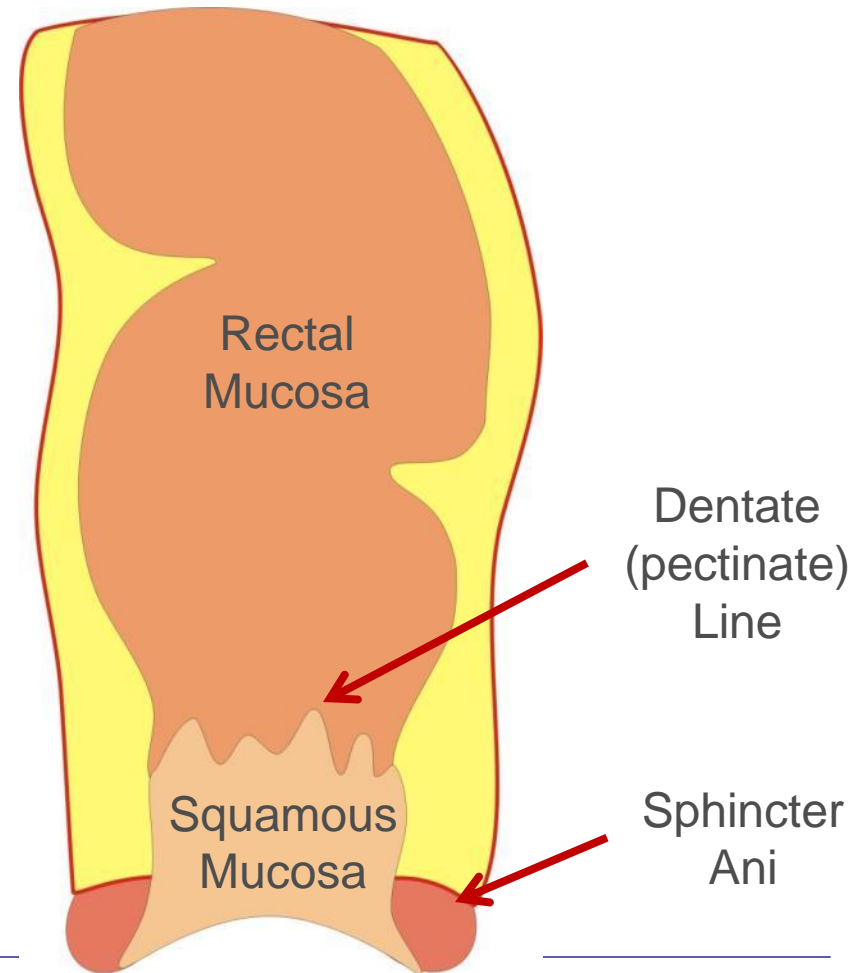
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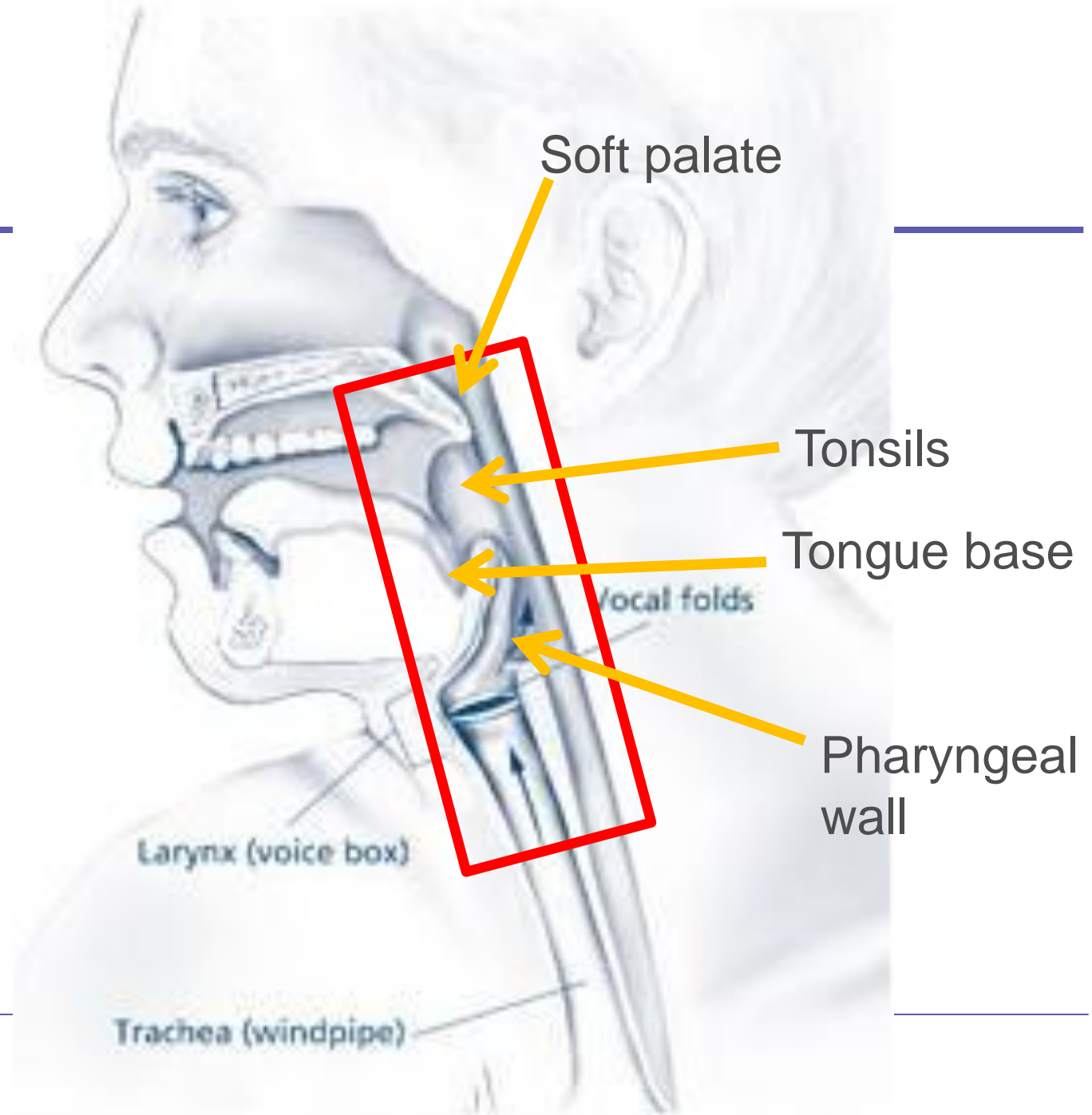
- Epithelia of body openings have stratified squamous epithelium
  - More internal areas have columnar epithelia
  - A band of rapidly dividing metaplastic cells (**transformation zone**) establishes a **squamo-columnar junction** somewhere near each body opening
  - Also occurs with lymphoid crypts
-

# Anal Anatomy

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- Anal t-zone morphologically analogous to the cervical Tzone
  - Variable region of squamous metaplasia
- Dentate line





# HPV Attributable Cancers

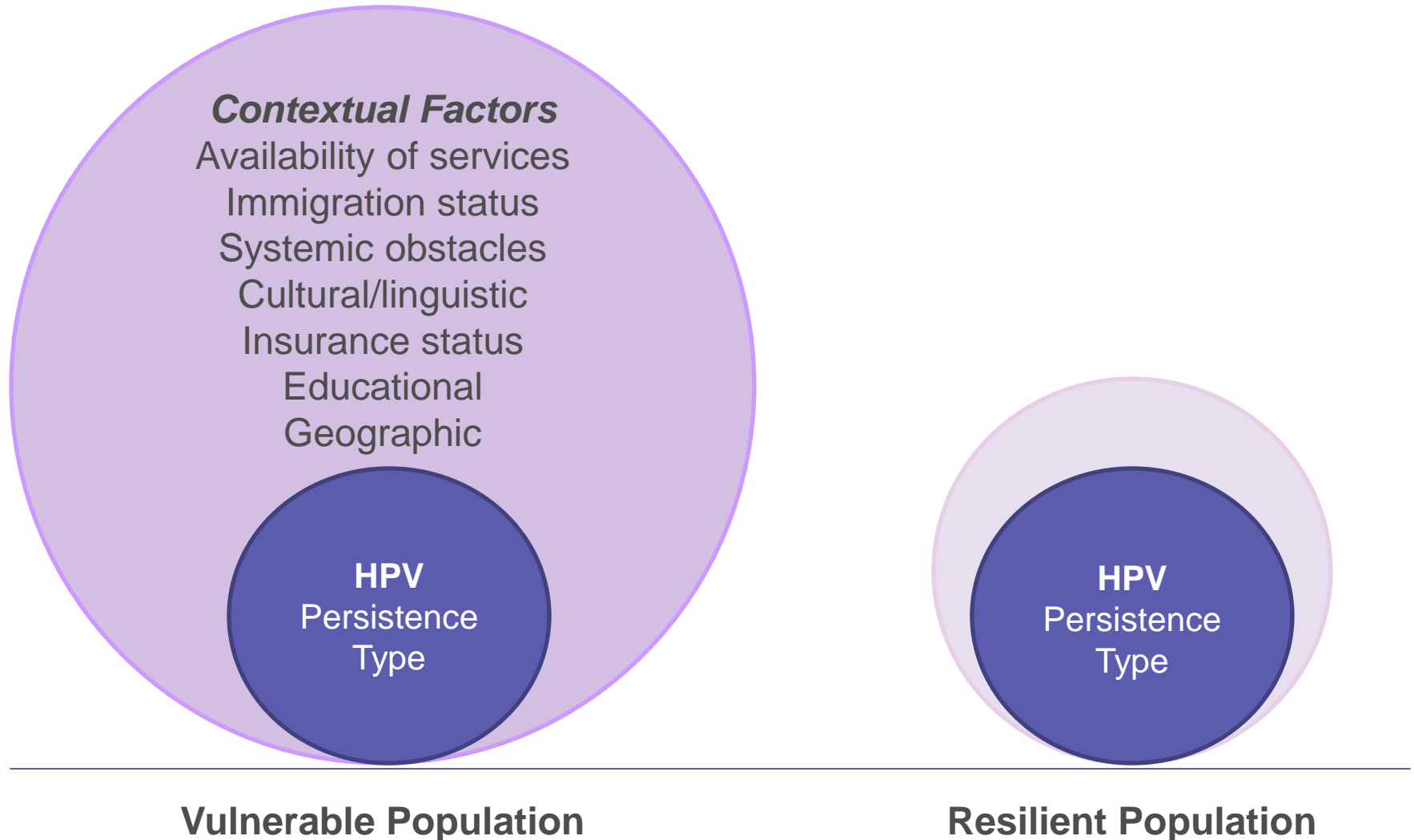
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(b) Gillison ML, Chaturvedi AK, Lowy DR. HPV prophylactic vaccines and the potential prevention of noncervical cancers in both men and women. Cancer. 2008;113(10 Suppl):3036–46.

# Relative Role of Host and Contextual Factors

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# Conclusion

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